OI Vey!

With their brave new immune systems, HAART-takers are eager to toss their prevention pills. Bob Lederer reports that the sky isn't falling.

May 1, 2001 By Bob Lederer

Jay Sheldrake of Carmel Valley, California, is a veteran of the AIDS-meds wars. After testing positive in 1988, he tried everything from approved antiretrovirals to a dizzying succession of underground "cures" to finally going cold turkey. As his CD4 count dropped to 200, his doctor had him begin the standard medications recommended for prevention (prophylaxis) of opportunistic infections (OIs), first for *Pneumocystis carinii* pneumonia (PCP), then for *Mycobacterium avium* complex (MAC) and finally for fungal infections. In the "bad old days," Sheldrake recalls, "I always had something -- swollen lymph nodes, thrush, diarrhea, whatever -- I saw myself wasting away and felt like the ax would fall at any moment." Indeed, in 1994, after an allergic reaction to the standard PCP prophylaxis TMP/SMX (Bactrim) forced a switch to aerosolized pentamadine, Sheldrake twice came down with a mild case of the then-common lung infection. Ultimately, he was able to reintroduce a lower Bactrim dose, fortified with a once-monthly pentamadine inhalation, both used as secondary prophylaxis (to prevent a recurrence), or "maintenance therapy," for what he assumed would be the rest of his life.

By 1997, after two years of HAART had boosted his CD4 count above 100 and greatly reduced his viral load, Sheldrake got his doctor's OK to stop the MAC prophylaxis. A few months later, as his CD4s cruised up into the mid-200s, the PWA pushed for something that was then considered highly risky -- going off PCP prophylaxis despite two previous bouts. "I'm fair-skinned, and the Bactrim made me hypersensitive," the compulsive tennis player says. "No matter how much sunblock I used, I always looked like a cherry." Other irritating side effects were dry, itchy skin, diarrhea and bloating. His doctor acquiesced, Sheldrake took the plunge, and no disaster ensued. Soon his doctor was pushing for this immune-reboostee to drop another drug, the fluconazole (Diflucan) he took to prevent fungal infections.

Sheldrake's journey to look-ma-no-prophy is an increasingly common one for HIVers lucky enough to have an in-the-know AIDS doctor. "It used to be that once you had an OI, you had to take prophylactic meds for life," says Judith Feinberg, MD, professor of medicine at the University of Cincinnati College of Medicine. "But there's been a dramatic shift: Even if you've had a bad OI, you can often go off those drugs once you've had a good response to antiretroviral treatment." That's great news for HIVers struggling to juggle pill-popping schedules, side effects and prescription bills. "Among people who get and adhere to good antiretroviral therapy, the risk of OIs is extraordinarily limited if not vanquished," Feinberg says.

While a federal panel signed off in 1999 on guidelines advising the withdrawal of *primary* (preventive) OI prophylaxis for those on HAART whose CD4s have bounced back (see "Prevention Suspension," *POZ*, February 2000), most doctors have been reluctant to do likewise with *secondary* post-OI diagnosis and treatment. But now a steady stream of data has persuaded cutting-edge physicians to push the envelope -- cautiously (see “Show Stoppers,” below). “Official guidelines are a catch-up mechanism for doctors with little hands-on experience,” says Feinberg, who sits on the federal panel. “If you have a wealth of experience, you’re probably ahead of the guidelines. That’s how this whole discontinuation practice came about -- people just started doing it.” Case in point: it took months of doctors and HIVers rebelling against the high side-effect load occasioned by the “hit hard, hit early” fervor before the feds finally revised the guidelines to support starting HAART at lower CD4s (see “The Lowdown”).

These latest findings about OI prophylaxis should keep you ahead of the curve:

PCP

Last January, two large European studies (325 and 113 HIVers) brought reassuring news: No one with a CD4 count above 200 who stopped secondary PCP prophylaxis suffered a relapse. “I feel comfortable stopping primary and secondary prophylaxis at the same CD4 counts and viral load levels,” says Joel Gallant, MD, professor of medicine and associate director of AIDS services at the Johns Hopkins University School of Medicine. Feinberg goes further: “The guidelines are outdated. We’ve been doing this for years and haven’t seen a relapse.”

MAC

A Canadian study found that after 17 months off MAC maintenance, only one of 33 PWAs relapsed -- and he had gone off HAART. “We often stop MAC secondary prophylaxis in those with immune reconstitution, but that’s not yet recommended,” says Gallant, who has seen no relapses in those with CD4s well above 100 and viral loads low or undetectable for six months or more.

Fungal Infections

"Physicians have created a big problem of resistant *Candida* through the excessive use of fluconazole [the leading drug for both prophylaxis and treatment],“ says Gallant. The result, he says, has been a range of fungal infections treatable only with the nightmarish drug amphotericin-B (Fungizone; HIVers dub its chills and fever ”shake ’n’ bake“). A study of PWAs on itraconazole (Sporanox) to prevent the fungal infection histoplasmosis, found a high rate of fungal resistance to both -azole drugs (see ”The Funky Fungus Among Us," *POZ*, September 2000). Gallant recommends sticking to the federal guidelines that limit secondary prevention for candidiasis only to those with frequent or severe bouts. “My experience is that immune reconstitution leads to protection against all these pathogens, even if they have caused disease in the past,” says Gallant. Meanwhile, a study last year found that acidophilus, a supplement made of beneficial intestinal bacteria that can prevent fungal overgrowth, has prophylactic effects comparable to antifungal drugs.

As for cryptococcal meningitis, Feinberg notes a new study showing cases in which secondary prophylaxis “is feasible to discontinue” -- 16 PWAs with an average CD4 count of 113 at

discontinuance; no relapses after 15 months. But she notes, “To make sure people are adequately protected, I would still not stop maintenance therapy until 150 or 200 CD4 cells -- after all, crypto is evil.”

In every case the decision to stop secondary prophylaxis is highly personal. “Once you’ve been hospitalized with a bad disease, you might become pretty conservative about how to be treated,” Feinberg says, emphasizing that the “complex decision” is based not only on CD4 counts but overall well-being and, especially, viral load. “All studies show that the people who do best are those with 5,000 or fewer copies.” And a brand-new French study found that because OIs still occur early in the course of HAART, HIVers should wait for at least four months into HAART and a dramatic CD4 rise before dropping any prophylaxis. Then there’s what Feinberg calls the “security blanket” factor: “This is the med that got you better, so you have to see whether you’re ready to fly without it.” In the end, she says, “Your doctor should provide as much information as possible, and you should be willing to be followed more closely.” That means taking standard blood work at least quarterly, more often if the person has an OI history or is on a HAART holiday.

Meanwhile, HIVers should also beef up their nutrient intake -- through diet and supplements -- as the best across-the-board prophylaxis: Nutrients play a vital role in immune function. A 1994 University of California at Berkeley study found higher nutrient levels correlated with much lower rates of PWA disease and death.

Today, Sheldrake, the ex-prophy popper, regrets not one moment of his multi-med history. “Being on those drugs held me together until HAART reconstituted my immune system,” he says. “But I’m absolutely relieved to be rid of those drugs,” particularly the antibiotics. “They’re really detrimental. I want my gut to be in the best shape it can be, so I can absorb as many nutrients as I can. And Bactrim’s pretty harsh over a lifetime.” Boasting a CD4 cell count of 350-and-counting and health that shines (save for a little lipodystrophy-induced paunch and a 42-year-old’s usual complaints), he lives every day free of OI fears. Tennis, anyone?

NEW OI PROPHYLAXIS GUIDELINES

SHOW STOPPERS *All recommendations are federal guidelines unless marked *; those come from leading HIV docs. All criteria for stopping prophylaxis include low or undetectable viral load for three to six months. -- Bob Lederer*

OI	**When to Start/Stop**		**Recommended Prophylaxis (from most to least effective)**	
	Primary	*Secondary*	*Primary*	*Secondary*
Candidiasis	not recommended	not recommended* (federal guideline is to start after frequent or severe recurrences)	acidophilus*	acidophilus*

Coccidioidomycosis	not recommended	Start: after case of disease; Stop: over 100-200 CD4s for 3-6 months*	not recommended	fluconazole; amphotericin B; itraconazole
Cryptococcal meningitis	not recommended	Start: after case of disease; Stop: over 100-200 CD4s for 3-6 months*	not recommended	fluconazole; amphotericin B; itraconazole
Cytomegalovirus (CMV)	not recommended (if below 50 CD4 cells and CMV positive, monitor eye health frequently)	Start: after case of CMV; Stop: over 100-150 CD4s for 3-6 months, but first consult with ophthalmologist	not recommended	Ganciclovir implant w/ oral ganciclovir; oral ganciclovir; foscarnet; cidofovir; fomivirsen injections
Herpes simplex virus	not recommended	Start: frequent or severe recurrences; Stop: significant CD4 rise above level of first outbreak*	acyclovir or famciclovir or valacyclovir***	acyclovir or famciclovir or valacyclovir***
Histoplasmosis	Start: under 100 CD4s, but beware toxicity, interactions, resistance; Stop: over 100 CD4s for 3-6 months*	Start: after case of disease; Stop: over 100-200 CD4s for 3-6 months*	itraconazole	itraconazole; amphotericin B
Mycobacterium avium Complex (MAC)	Start: under 50 CD4s; Stop: over 100 CD4s for 3-6 months	Start: after case of disseminated MAC; Stop: over 100-200 CD4s for 3-6 months*	azithromycin; clarithromycin; rifabutin; azithromycin/ rifabutin	clarithromycin/ ethambutol; azithromycin/ ethambutol, w/ or w/out rifabutin
Pneumocystis carinii pneumonia (PCP)	Start: under 200 CD4s or 14 percent CD4s or AIDS-defining illness; Stop: over 200 CD4s for 3-6 months	Start: after case of disease; Stop: over 200 CD4s for 3-6 months*	TMP-SMX (Bactrim or Septra);** dapsone; aerosolized pentamidine; atovaquone	TMP-SMX (Bactrim or Septra);** dapsone; aerosolized pentamidine; atovaquone

Toxoplasmosis (note: prophylaxis against PCP will also protect against toxo)	Start: under 100 CD4s and toxo antibody; Stop: over 200 CD4s for 3-6 months*	Start: after case of disease; Stop: brain MRO shows disease resolution over 200 CD4s for 3-6 months*	TMP-SMX (Bactrim or Septra);** dapsone/ pyrimethamine; atovaquone w/ or w/out pyrimethamine	sulfadizine/ pyrimethamine/ leucovorin; clindamycin/ pyrimethamine/ leucovorin; atovaquone (or azithromycin*) w/ or w/out pyrimethamine/ leucovorin
Tuberculosis	Start: positive PPD skin test with no active TB; or recent contact with infectious TB patient;Stop: at end of 2-9-month treatment	not recommended	depends on presence of drug resistance and other meds taken; see specialist	not recommended

SOURCES: 1999 USPHS/IDSA Guidelines for the Prevention of Opportunistic Infections in Persons Infected with HIV, available at www.hivatis.org or www.amfar.org/td; interviews with and articles by leading HIV physicians. Not included here are recommended vaccinations to prevent varicella zoster cirus, streptococcal pneumonia, hepatitis A or B and influenza. In addition, some doctors recommend lifelong prophylaxis with the antiherpes drugs listed above to help prevent non-Hodgkin's lymphoma.

**If you overcame an earlier allergic reaction to Bactrim or Septra, there is a chance that you may be allergic when you resume the drug. Discuss this with your physician.

***If separated by "or," options are considered equally effective.
